REMARKS

Claims 1-5 are in this case.

Claim Objections

Concerning the formal objections to the claims raised by the Examiner, the missing periods at the end of claims 1, 3, 4 and 5 have been supplied.

Claim Rejections – 35 U.S.C. § 112

Claim 3 has been amended by deleting "; and, if desired," and deleting step d).

Claim Rejections – 35 U.S.C. § 102

Applicants respectfully disagree with the examiner's view that route b) of claims 1 and 3 and route d) of claim 1 lack novelty over *Masciadri*, U.S. Patent 5,773,446.

Claim 1 recites a process for synthesizing the compound of Formula I involving a novel cyclisation method for introducing the chromen ring starting from compound 1. This novel cyclisation step serves to synthesise the intermediates of Formula 2 used in steps a) and b) as well as intermediate 5 in step c). Even if *Masciadri* were deemed to disclose (see columns 5 and 6) a possibly known method for reducing a benzylic ester to the corresponding aldehyde, the reference does not disclose the specific combination of reactions in the present application, for example, the synthesis of a compound of Formula 2 via step A1 and further reduction/oxidation of said obtained compound 2.

Considering the compound of Formula III in *Masciadri*, this reference only discloses in columns 3 and 6 that a compound of Formula III (analogous to the compound of Formula 11 of the present invention) can be obtained according to known methods. However, *Masciadri* does not disclose that the present compound of Formula 11 can be obtained starting from compound 1 or 6 involving a cyclisation step A1 or A2 and further steps such as A4. The combination of reaction

steps of applicants' process to obtain the compound of Formula I is not disclosed in *Masciadri*. Only the present process discloses the synthesis of the compound of Formula I via this specific succession of reaction steps. Therefore, it must be concluded that the subject matter of claim 1 is patentably novel over *Masciadri*.

A similar argument can be made with respect to applicants' claim 3. None of the prior art references discloses a process for synthesising the compound of Formula 5 involving the cyclisation step A1 or A2. Therefore, the reaction steps constituting the subject matter of claim 3 is novel over *Masciadri*`.

Claim Rejections – 35 U.S.C. § 103

1. Obviousness Rejections of Claims 1-3 Over *Masciadri* in View of EP 0 629 619

Applicants respectfully disagree with the examiners contention that the subjects matter of claims 1 to 3 are obvious over *Masciadri* in view of EP 0 629 619.

The present application provides a process for synthesizing the compound of Formula I with a high overall yield and with a reduced number of reaction product isolation steps. It provides a process wherein the intermediate compound of Formula 5 is synthesized by a novel cyclisation step (see claims 1 and 3, steps a) and c)). Furthermore, the application provides a synthesis of the compound of Formula I in high yield and high purity without the use of chromatography (see the experimental portion of the specification).

Masciadri, which is represented as being the closest prior art, does not reveal any cyclisation such as the one disclosed in the present application. Furthermore, the process of *Masciadri* only exemplifies synthetic methods involving cumbersome chromatography to obtain compound I and its intermediates. Therefore, no teaching is provided in *Masciadri* for obtaining the compound of Formula I in high yields and without requiring chromatography. Consequently, applicants submit that the subject matter of their application is non-obvious over *Masciadri*.

EP 0 629 619 discloses a cyclisation involving an acetal having the Formula 1,1-dialkoxy-3-methyl-2-buten and a phenol which can have up to 2 substituents. However, nothing in EP 0 629 619 indicates that the cyclisation disclosed therein could be applied to a phenol having up to 3 substituents at the 2, 3 and 5 positions of the phenol, together with the present acetal 9. One of ordinary skill in the art would not have been inspired to apply the cyclisation disclosed in EP 0 629 619 together with the alternative preparation of *Masciadri* in order to synthesise the compound of Formula I in high yield and without the use of chromatography. Neither EP 0 629 619 nor *Masciadri* indicates that such a combination of steps would succeed. Furthermore, neither reference discloses the synthesis of the acetal 9 involved in the cyclisation according to the present application. Before even considering the process of *Masciadri* in combination with the teaching of EP 0 629 619, one of ordinary skill in the art would need to know how to synthesise efficiently the intermediate of Formula 9 which is not taught in the cited prior art.

In view of the foregoing, applicants respectfully submit that the subjects matter defined in claims 1-3 are non-obvious in view of *Masciadri* alone or in combination with EP 0 629 619.

2. Obviousness Rejection of Claim 4 Over *Masciadri*

The examiner considers it obvious to one of ordinary skill in the art that the ester of Formula 2 in *Masciadri* can be alternatively converted to the carbaldehyde of Formula 5 via the acid 3 of applicants' claim 4.

However, *Masciadri* does not disclose any process involving an additional saponification step and the synthesis of the compound of Formula 3. The use of this intermediate 3 in the present process cannot be obvious to one of ordinary skill in the art. Applicants have solved the problem of synthesizing the compound of Formula I in high yield by a minimal number of steps and without involving any expensive and cumbersome purification or isolation step. However, introducing the compound of Formula 3 and consequently an additional step in a process could represent a risk of lowering the overall yield for obtaining the compound of Formula I. This compound of Formula 3 is introduced just after the cyclisation reaction which is performed under drastic conditions such as

in high boiling solvents in the presence of a base and at a temperature range of 100°C to 170°C. Under such reaction conditions it might be difficult to isolate the desired reaction product from by-products and residual solvents without involving expensive and cumbersome purification steps. However, as exemplified in Example 3, the acid intermediate 3 of the present invention is surprisingly obtained in high yield and purity without involving cumbersome purification steps.

Furthermore, *Masciadri* does not teach the introduction of an additional intermediate acid 3 to improve the overall yield of the compound of Formula I. Therefore, it would not occur to one of ordinary skill in the art, having the benefit of the teaching in *Masciadri*, to introduce an additional intermediate into the present process. Only the present invention provides the introduction of novel intermediate 3 into the process to enable the compound of Formula I to be obtained in high yield and purity without resorting to any chromatography. Therefore, it is respectfully submitted that the compound 3 of present claim 4 is not considered being obvious in view of *Masciadri*.

Allowable Subject Matter

Claim 5 is herein amended to overcome the objection stated above, and should therefore be allowed.

Conclusion

In view of the foregoing amendments and remarks, applicants respectfully submit that all of the grounds stated in the Office action for withholding allowance of the present application have

been fully met, and that the case should therefore be passed to issuance. If the examiner believes it would advance the prosecution of this case, he is invited to 'phone the undersigned at the number below indicated.

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Respectfully submitted,

JURGEN JAEGER, KASPAR BURRI,
SORANA GREIVELDINGER-POENARU, and
JOHANNES HOFFNER, Applicants

By_____
Charles E. Miller
Registration No.: 24,576
DICKSTEIN SHAPIRO LLP
1633 Broadway
New York, New York 10019-6708
(212) 277-6500
Attorney for Applicant